

> S 14 AND L7  
L15 81 L14 AND L7

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=> D 1-81 TI

=> S SEQUENCE/TI  
72256 SEQUENCE/TI  
37008 SEQUENCES/TI  
L16 107231 SEQUENCE/TI  
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=> S L16 AND L13  
L17 477 L16 AND L13

=> S L16 AND L14  
L18 136 L16 AND L14

=> D 1-136 TI

=> D 37,53 CBIB ABS

L18 ANSWER 37 OF 136 CAPLUS COPYRIGHT 2003 ACS on STN  
2000:388525 Document No. 133:39121 \*\*\*Sequences\*\*\* of homologs (NL2,  
NL3, and NL6) of known ligands of TIE receptor \*\*\*tyrosine\*\*\*  
\*\*\*kinase\*\*\*. Fong, Sherman; Ferrara, Napoleone; Goddard, Audrey;  
Godowski, Paul J.; Gurney, Austin L.; Hillan, Kenneth; Williams, P. Mickey  
(Genentech, Inc., USA). U.S. US 6074873 A 20000613, 50 pp.,  
Cont.-in-part of U.S. Ser. No. 934,494. (English). CODEN: USXXAM.  
APPLICATION: US 1998-143068 19980828. PRIORITY: US 1997-934494 19970919.  
AB The invention provides protein and cDNA sequences of homologs (NL2, NL3,  
and NL6) of known ligands of TIE receptor tyrosine kinase. NL3 has a  
fibrinogen-like domain, has homol. with human TL-1 and human TL-2, and it  
is of particular interest in this invention. The invention also relates  
to the effects the provided TIE ligand homologs, esp. NL3, have on cell  
proliferation, apoptosis, and angiogenesis.

L18 ANSWER 53 OF 136 CAPLUS COPYRIGHT 2003 ACS on STN  
1998:187324 Document No. 128:266352 Homologous \*\*\*sequences\*\*\* in the  
primary structures of \*\*\*tyrosine\*\*\* \*\*\*kinase\*\*\* receptors of the  
insulin superfamily and protein-substrates 1 and 2 of the insulin  
receptor. Shpakov, A. O. (I.M. Sechenov Institute of Evolutionary  
Physiology and Biochemistry, Russian Academy of Sciences, Russia).  
Ukrainskii Biokhimicheskii Zhurnal, 69(4), 39-48 (Russian) 1997. CODEN:  
UBZHD4. ISSN: 0201-8470. Publisher: Institut Biokhimii im. A. V.  
Palladina NAN Ukrainy.

AB Ligand-activated tyrosine kinase receptors of insulin superfamily peptides  
can realize the signal transduction to the SH2-proteins  
phosphatidylinositol 3-kinase (PI3K), protein phosphotyrosine phosphatase  
(PPTP), and GRB2-adaptor protein via 2 pathways: (1) with participation of  
specific proteins, the insulin receptor substrates 1 and 2 (IRS1/IRS2);  
and (2) direct interaction between receptors and SH2-proteins (without  
IRS-proteins). Consequently, structurally related determinants, which are  
responsible for the interaction with SH2-proteins, must be present in the  
receptor and IRS mols. The comparative anal. of amino acid sequences  
(AAS) of human receptors for insulin, insulin-like growth factor-I and  
insulin-related peptide and AAS of IRS1/IRS2 proteins allow one to  
identify for the first time the long homologous regions in their primary  
structures. After alignment of AAS of the regions, the sited-targets for  
tyrosine phosphorylation, most important for functional activity of  
tyrosine kinase receptors and IRS proteins, coincided with each other.  
These results show that some homologous regions can have similar function.  
Thus, the regions can be involved in coupling the receptors and  
IRS-proteins with SH2-proteins, such as PI3K, PPTP, GRB2-adaptor protein.  
It is also possible that the homologous regions of tyrosine kinase  
receptors and IRS1/IRS2 proteins mediate the interaction between their  
proteins.